Pseudomonas colicin M-type bacteriocins target different TonB-dependent outer-membrane proteins

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Micro-organisms are equipped with an armamentarium of secreted antibacterial proteins to harness themselves in competitive environments. A major subset of these bacteriocins are synthesized as modular proteins and include a receptor-binding domain, a membrane translocating motif and a toxin-immunity module at the C-terminus. Bacteriocins equipped with a colicin M (ColM) toxin domain kill target cells via degradation of lipid II, hereby impeding peptidoglycan biosynthesis.

We performed a comprehensive *in silico* analysis for the presence of ColM modules in proteobacterial genomes. In addition to identifying two ColM-type bacteriocin organizations with a dual toxin architecture, phylogenetic analysis indicated that ColM modules fall apart in two distinct clusters. ColM bacteriocins originating from *Escherichia coli* and other *Enterobacteriaceae* are consistently equipped with a *cmi*-type immunity gene, whereas immunity to ColM-type bacteriocins from other genera is displayed by a distinct set of small proteins with different transmembrane helix topologies. The complete lack of sequence similarity of the predicted receptor-binding domains of ColM-type bacteriocins from different genera suggests that these bacteriocins have recruited different outer-membrane targets to gain access to target cells. Using recombinantly-produced proteins and a transposon mutagenesis approach of susceptible cells, we show that ColM bacteriocins in *Pseudomonas* target at least two different TonB-dependent outer-membrane proteins, both involved in the uptake of iron via siderophores.

Together, our results demonstrate that colicin M-type bacteriocins are truthful polymorphic toxins that have been subject of intensive recombination events. The piracy of receptors involved in iron uptake highlights the critical role of this compound in niche colonization.